REMARKS

Claims 61-67 are pending.

Priority

The Office Action states that "[a]pplicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C 119(e)." Applicants respectfully disagree.

Both disclosures in the provisional application 60/024,845 (the "'845 provisional") and the instant application that claims priority to this provisional provide full support for pending claims. This support is shown graphically in Appendix A, showing a nucleotide sequence alignment and Appendix B, showing a protein alignment, both attached herewith for the Examiner's convenience. These appendices label sequences disclosed in the '845 provisional as '845Prov. The sequence disclosed in the instant application is labeled '043. The appendices also align SEQ ID 772 of Kunsch, discussed infra.

The sequence alignments show, contrary to the Examiner's assertion, that claim 61, reciting in part a nucleotide sequence that hybridizes under stringent conditions to a complementary strand of a polynucleotide having SEQ ID 1, is fully supported by the disclosure in the '845 provisional. The '845 provisional discloses a nucleotide sequence that differs from SEQ ID NO: 1 by only three nucleotides. Further, as the Examiner notes, for a nucleotide sequence to hybridize to SEQ ID NO: 1, as recited in claim 61, the nucleotide sequence need not be complementary over the entire length. Office Action p. 7 ll. 7-9.

The protein sequence alignment between the '845 provisional and the instant disclosure differs by only one residue at the C-terminal, as the Examiner notes. The nucleotide and protein sequence disclosed in the '845 provisional therefore fully supports claim 61 which also recites, in part, a nucleotide encoding a polypeptide comprising an amino acid sequence having at least 95% identity to the amino acid sequence set forth in SEQ ID NO:2.

Rejection of claims under 35. U.S.C. 112

Claims 61-67 stand rejected under 35 U.S.C. 112, first paragraph. The Examiner asserts that because the specification, while being enabled for an isolated nucleic acid sequence comprising a nucleotide sequence that encodes a polypeptide that reduces crotonyl-CoA or

crotonyl-ACP and comprises an amino acid sequence either identical to SEQ ID NO: 2, or differing from SEQ ID NO:2 by substitution, insertion or deletion of a single amino acid, does not reasonably provide enablement for a nucleotide sequence encoding a polypeptide that reduces crotonyl-CoA or crotonyl-ACP and differs from SEQ ID NO:2 by insertion, deletion or substitution [of] more than one amino acid. The Examiner indicates that this rejection relates to parts (d) and (e) of claim 61, part (g) of claim 61 as it relates to parts (d) and (e), and claims 62-67 as these claims relate to parts (d) and (e). Applicants respectfully traverse this rejection.

It is a well-settled tenet of patent law that "mere breadth" is not a proper test under 112 first paragraph. See, In re Marzocchi et al., 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). Furthermore, the Federal Circuit has also held that a "patent specification [is] enabling even though it listed elements that could form thousands of end products, some of which may not be operative." Atlas Powder Co. V. E.I. du Pont de Nemours & Co., 224 U.S.P.Q. 409 (Fed. Cir. 1984). Accordingly, even if the claims were to read on some inoperative embodiments the law states that the specification would still meet the requirements of section 112.

Applicants note that a long pedigree of cases have held that there is no requirement of *a priori* knowledge of all specific embodiments of the claimed invention. Enablement is not precluded even if some experimentation is necessary. Applicants contend that the specification provides sufficient guidance with respect to polypeptides that reduce crotonyl-CoA or crotonyl-ACP, such that a person of ordinary skill in the art could make and use the claimed nucleotide sequences without undue experimentation, relying on the specification and knowledge in the art. The teachings of the specification clearly enable the skilled artisan to make and use a vast range of hybrid polypeptides at least for the following reasons.

The Examiner asserts that "the specification contains no guidance or citations of relevant prior art that would inform the skilled artisan of which amino acid residues of SEQ ID NO: 2 could be altered without adversely affecting its folding or biological activity." Applicants respectfully submit that, a person of skilled in the art, can readily determine whether a polypeptide as recited in claim 61 is capable of reducing crotonyl-CoA or crotonyl-ACP using for example, the enzyme activity analysis disclosed in the instant specification at for example, page 52 ll. 20-28, Example 2, and page 42 ll. 17-25 describing screening for detection of the reduction of crotonyl-CoA by measuring the consumption of NADH.

Additionally, Applicants respectfully remind the Examiner that "[a] specification is presumed to be enabling and the U.S. Patent and Trademark Office (PTO) has the burden of establishing a prima facie case of lack of enablement." In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976). To make a prima facie case of lack of enablement, the PTO must come forward with reasons, supported by the record as a whole, showing why the specification fails to enable one of ordinary skill in the art to make and use the claimed invention. Id. The burden is on the PTO to establish that experimentation would be undue, taking into consideration the eight factors that are to be considered in determining whether a disclosure requires undue experiment. In re Wands, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). In applying these eight factors to the instant case it is evident from the above discussion that the level of skill in this art was very high at the time the application was filed, and the experimental techniques needed to practice the invention were well known and exemplified in the specification as filed. Accordingly, Applicants respectfully submit that armed with the teachings of the specification and the contemporary knowledge in the art, the skilled artisan would be able to practice the claimed invention without further undue experimentation.

Screening techniques taught in the specification combined with those techniques available in the art at the time the present invention was made provide sufficient guidance for generating nucleotide sequences that both encode the recited polypeptides and are capable of reducing crotonyl-CoA or crotonyl-ACP, as recited in claim 61. Accordingly, Applicants assert that the specification, in light of the art at the time the present invention was made, is enabling for a sufficient number of other permutations of the claimed nucleotide sequences to entitle Applicants to the invention as presently claimed. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of claims under 35 U.S.C. § 102(e)

Claims 61-67 were rejected under 35 U.S.C. § 102(e) as being anticipated by Kunsch et al. (U.S. Patent No. 6,593,114), which claims priority through U.S.S.N. 08/781,986 filed 1/3/1997. The Office Action states that Kunsch et al. discloses a polynucleotide comprising SEQ ID NO: 772 and that "[n]ucleotides 24-704 of SEQ ID NO: 772 correspond[] to nucleotides 1-678 of instant SEQ ID NO: 1." The rejection is respectfully traversed.

Applicants assert that U.S. Patent No. 6,593,114 is not a proper reference under 35 U.S.C. § 102(e) because the earliest priority date for that patent which supports the subject matter used to make this rejection will fall after Applicants' earliest filing date (August 28, 1996). As Applicants note above, the priority document fully supports claims 61-67. In particular, the priority document discloses a sequence with more than 95% identity over the corresponding claimed sequence region. Therefore, the earliest filing date of the instant application is August 28, 1996, and as such U.S. Patent No. 6,593,114 does not qualify as prior art under 35 U.S.C. § 102(e). Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Double Patenting

Claims 61-67 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,432,670. Applicants respectfully request that the Examiner hold in abeyance this rejection until allowable subject matter is indicated.

Conclusion

In view of the above remarks and the amendments to the claims, it is believed that this application is in condition for allowance. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

By: _____
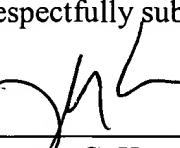
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COMPARISON OF NUCLEIC ACID SEQUENCES
APPENDIX A

CLUSTAL

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'043      ------------------------------------------------------------
'845Prov  ATATGATATTAAAATGCAGGAACGTATT-AGTACGAACGTAAAATTAATGATTTAAAATG    59
Kun772    ------------------------------------------------------------


'043      ------------------------------------------------------------
'845Prov  CTAGTATGTATATGATTTTGATAAATAAATGCTTTTTAACGTAAATCAAGTTTGATACAG   119
Kun772    ------------------------------------------------------------


'043      ------------------------------------------------------------
'845Prov  AAAGGACTAAATCAAACATTTATTCGTTGTAATAACGTTTAAATAACTTTATTAAAAAG    179
Kun772    ------------------------------------------------------------


'043      ------------------------------------------------------------
'845Prov  TCATAATAGTGTTAAAATGTATTGACGAATAAAAAGTTAGTTAAAACTGGGATTAGATAT   239
Kun772    ------------------------------------------------------------


'043      -----------------------------------------ATGTTAAATCTTGAAAACAA    20
'845Prov  TCTATCCGTTAAATTAATTATTATAAGGAGTTATCTTAACATGTTAAATCTTGAAAACAA   299
Kun772    ---------------ATTATTATAAGGAGTTATCTTA-CATGTTAAATCTTGAAAACAA    43


'043      AACATATGTCATCATGGGAATCGCTAATAAGCGTAGTATTGCTTTTGGTGTCGCTAAAGT    80
'845Prov  AACATATGTCATCATGGGAATCGCTAATAAGCGTAGTATTGCTTTTGGTGTCGCTAAAGT   359
Kuns772    AACATATGTCATCATGGGAATCGCTAATAAGCGTAGTATTGCTTTTGGTGTCGCTAAAGT   103


'043      TTTA-GATCAATTAGGTGCTAAATTAGTATTTACTTACCGTAAAGAACGTAGCCGTAAAG   139
'845Prov  TTTA-GATCAATTAGGTGCTAAATTAGTATTTACTTACCGTAAAGAACGTAGCCGTAAAG   418
Kun772    TTTA-GATCAATTAGGTGCTAAATTAGTATTTACTTACCGTAAAGAACGTAGCCGTAAAG   162


'043      AGCTTGAAAAATTATTAGAACAATTAAATCAACCAGAAGCGCACTTATATCAAATTGATG   199
'845Prov  AGCTTGAAAAATTATTAGAACAATTAAATCAACCAGAAGCGCACTTATATCAAATTGATG   478
Kun772    AGCTTGAAAAATTATTAGAACAATTAAATCAACCAGAAGCGCACTTATATCAAATTGATG   222


'043      TTCAAAGCGATGAAGAGGTTATTAATGGTTTTGAGCAAATTGGTAAAGATGTTGGCAATA   259
'845Prov  TTCAAAGCGATGAAGAGGTTATTAATGGTTTTGAGCAAATTGGTAAAGATGTTGGCAATA   538
Kun772    TTCAAAGCGATGAAGAGGTTATTAATGGTTTTGAGCAAATTGGTAAAGATGTTGGCAATA   282


'043      TTGATGGTGTATATCATTCAATCGCATTTGCTAATATGGAAGACTTACGCGGACGCTTTT   319
'845Prov  TTGATGGTGTATATCATTCAATCGCATTTGCTAATATGGAAGACTTACGCGGACGCTTTT   598
Kun772    TTGATGGTGTATATCATTCAATCGCATTTGCTAATATGGAAGACTTACGCGGACGCTTTT   342


'043      CTGAAACTTCACGTGAAGGCTTCTTGTTAGCTCAAGACATTAGTTCTTACTCATTAACAA   379
'845Prov  CTGAAACTTCACGTGAAGGCTTCTTGTTAGCTCAAGACATTAGTTCTTACTCATTAACAA   658
Kun772    CTGAAACTTCACGTGAAGGCTTCTTGTTAGCTCAAGACATTAGTTCTTACTCATTAACAA   402


'043      TTGTGGCTCATGAAGCTAAAAAATTAATGCCAGAAGGTGGTAGCATTGTTGCAACAACAT   439
'845Prov  TTGTGGCTCATGAAGCTAAAAAATTAATGCCAGAAGGTGGTAGCATTGTTGCAACAACAT   718
Kun772    TTGTGGCTCATGAAGCTAAAAAATTAATGCCAGAAGGTGGTAGCATTGTTGCAACAACAT   462


'043      ATTTAGGTGGCGAATTCGCAGTTCAAAATTATAATGTGATGGGTGTTGCTAAAGCGAGCT   499
'845Prov  ATTTAGGTGGCGAATTCGCAGTTCAAAATTATAATGTGATGGGTGTTGCTAAAGCGAGCT   778
Kun772    ATTTAGGTGGCGAATTCGCAGTTCAAAACTATAATGTGATGGGTGTTGCTAAAGCGAGCT   522


'043      TAGAAGCAAATGTTAAATATTTAGCATTAGACTTAGGTCCTGATAATATTCGCGTTAATG   559
'845Prov  TAGAAGCAAATGTTAAATATTTAGCATTAGACTTAGGTCCTGATAATATTCGCGTTAATG   838
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Kun772     TAGAAGCAAATGTTAAATATTTAGCATTAGACTTAGGTCCAGATAATATTCGCGTTAATG      582

'043       CAATTTCAGCTGGTCCAATCCGTACATTAAGTGCAAAAGGTGTGGGTGGTTTCAATACAA      619
'845Prov   CAATTTCAGCTGGTCCAATCCGTACATTAAGTGCAAAAGGTGTGGGTGGTTTCAATACAA      898
Kun772     CAATTTCAGCTAGTCCAATCCGTACATTAAGTGCAAAAGGTGTGGGTGGTTTCAATACAA      642

'043       TTCTTAAA-GAAATCGAAGAGCGTGCACCTTTAAAA--CGTAACGTTGATCAAGTAGAAG      676
'845Prov   TTCTTAAA-GAAATCGAAGAGCGTGCACCTTTAAAA--CGTAACGTTGATCAAGTAGAAG      955
Kun772     TTCTTAAA GAAATCGAAGAGCGTGCACCTTTTAAA CGTAATGTTGATCCAGTAGAAG      702

'043       TAGGTAAAACAGCGGCTTACTTRTTAAGTGACTTATCAAGTGGCGTTACAGGTGAAAATA      736
'845Prov   TAGGTAAAACAGCGGCTTACTTATTAAGTGACTTATCAAGTGGCGTTACAGGTGAAAATA     1015
Kun772     TA----------------------------------------------------------      704

'043       TTCATGTAGATAGCGGATTCCACGCAATTAAATAA-------------------------      771
'845Prov   TTCATGTAGATAGCGGATTCCACGCAATTAATAATATCATTCAACAGCTTGGGTTCACCG     1075
Kun772     ------------------------------------------------------------

'043       ------------------------------------------------------------
'845Prov   TTTATCATATATTGTGGAGCAAAAGCTTTNTGGGTTTTATTAATAATCNGGCTGATGGAA     1135
Kun772     ------------------------------------------------------------

'043       ------------------------------------------------------------
'845Prov   AATTATTGGATATTTCAACCTGACTTGATT------------------------------     1165
Kun772     ------------------------------------------------------------
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Key:
'043   = SEQ ID NO: 1 from U.S. Application No. 08/790,043 to Payne et al.
'845Prov = SEQ ID NO: 1 from U.S. Provisional App. No. 60/024,845 to Payne et al.
Kun772   = SEQ ID NO: 772 from EP Application No. 0786519 to Bailey et al.

Yellow highlight = start/stop codons
Green highlight = nucleotide changes as compared to '043
█████████ = nucleotide insertions as compared to '043

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COMPARISON OF AMINO ACID SEQUENCES
APPENDIX B

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CLUSTAL

'043     MLNLENKTYVIMGIANKRSIAFGVAKVLDQLGAKLVFTYRKERSRKELEKLLEQLNQPEA     60
'845Prov MLNLENKTYVIMGIANKRSIAFGVAKVLDQLGAKLVFTYRKERSRKELEKLLEQLNQPEA     60
Kun772   MLNLENKTYVIMGIANKRSIAFGVAKVLDQLGAKLVFTYRKERSRKELEKLLEQLNQPEA     60


'043     HLYQIDVQSDEEVINGFEQIGKDVGNIDGVYHSIAFANMEDLRGRFSETSREGFLLAQDI    120
'845Prov HLYQIDVQSDEEVINGFEQIGKDVGNIDGVYHSIAFANMEDLRGRFSETSREGFLLAQDI    120
Kun772   HLYQIDVQSDEEVINGFEQIGKDVGNIDGVYHSIAFANMEDLRGRFSETSREGFLLAQDI    120


'043     SSYSLTIVAHEAKKLMPEGGSIVATTYLGGEFAVQNYNVMGVAKASLEANVKYLALDLGP    180
'845Prov SSYSLTIVAHEAKKLMPEGGSIVATTYLGGEFAVQNYNVMGVAKASLEANVKYLALDLGP    180
Kun772   SSYSLTIVAHEAKKLMPEGGSIVATTYLGGEFAVQNYNVMGVAKASLEANVKYLALDLGP    180


'043     DNIRVNAISAGPIRTLSAKGVGGFNTILKEIEERAPLKRNVDQVEVGKTAAYLLSDLSSG    240
'845Prov DNIRVNAISAGPIRTLSAKGVGGFNTILKEIEERAPLKRNVDQVEVGKTAAYLLSDLSSG    240
Kun772   DNIRVNAISASPIRTLSAKGVGGFNTILKRNRRACTFNRNVDEVEV-------------    226


'043     VTGENIHVDSGFHAIK-----------------------------------    256
'845Prov VTGENIHVDSGFHAINXTIQOLGFTVYHILWSKSFXGFINNXADGKLLDIST    292
Kun772   ---------------------------------------------------
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Key:
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'043     = SEQ ID NO: 2 from U.S. Application No. 08/790,043 to Payne et al..
'845Prov = SEQ ID NO: 2 from U.S. Provisional App. No. 60/024,845 to Payne et al.
Kun772   = Translation of SEQ ID NO: 772 from Kunsch et al.
Green highlight = amino acid changes as compared to '043
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